

**Reissue Declaration by Inventor**

The Examiner rejected all claims under 35 U.S.C. 251 as being improperly broadened without support of a Declaration by the Inventor.

Please find attached a fully executed Reissue Declaration by the Inventor. In view of this attachment, Applicant submits that the above rejection has been overcome and respectfully requests that it be withdrawn.

**Computer Readable Form of Sequence Listing**

Applicant gratefully acknowledges the Examiner's comments in regard to using the computer readable form of the sequence listing of patent 5,654,413. A request to transfer the computer readable form from that file is attached.

**Information Disclosure Statement**

Applicant gratefully acknowledges the Examiner's comments in regard to references cited in patent 5,654,413. Attached is a Supplemental Information Disclosure Statement citing the references listed in that patent.

**Double Patenting**

The Examiner provisionally rejected claims 5, 7, and 9 under the doctrine of obviousness-type double patenting with respect to claims 73, 77, and 78 of co-pending application 09/092,226.

Please find attached a Terminal Disclaimer under 37 C.F.R. 1.321(c) in respect of co-pending application 09/092,226.

The Examiner provisionally rejected claims 1-4 under the doctrine of obviousness-type double patenting with respect to claims 46-52 of co-pending application 09/183,650.

Please find attached a Terminal Disclaimer under 37 C.F.R. 1.321(c) in respect of co-pending application 09/183,650.

In view of the attached Terminal Disclaimers, Applicant submits that the Examiner's concern in regard to double patenting has been addressed and respectfully requests that the above rejections be withdrawn.

**Rejection under 35 U.S.C. 112 Second Paragraph**

The Examiner rejected claim 8 under 35 U.S.C. 112 second paragraph for confusion regarding whether the word "size" refers to length of cDNAs in a population or the number of cDNAs in a population.

Applicant respectfully disagrees with the rejection in view of the above amendments. Applicant submits that it is now clear that size refers to the *number* of cDNAs in the population.

### Rejection under 35 U.S.C. 102

The Examiner rejected claim 5 under 35 U.S.C. 102(b) as being anticipated by Dower et al for its disclosure of a population of microparticles having attached synthetic oligonucleotide, wherein substantially all different synthetic oligonucleotides are attached to different microparticles.

Applicant respectfully disagrees with this rejection in view of the amendment to claim 5. Dower at most discloses mixtures of microparticles with *synthetic* oligonucleotides attached such that different synthetic oligonucleotides are attached to different microparticles, which is the result of a "split and mix" synthetic approach, as illustrated in Figures 1 and 2 of the reference. Claims 5, as amended, is directed to microparticles having *non-synthetic* polynucleotides attached; namely, cDNAs and genomic DNA fragments. This distinction is important because microparticles having such polynucleotides attached are neither disclosed nor suggested by Dower. It is also important that the purpose of the oligonucleotides in Dower is to encode, or provide an "identifier tag," for the synthetic steps used to create oligomers that are co-synthesized on the microparticles. Non-synthetic polynucleotides such as cDNAs or genomic DNA fragments are clearly not useful for such a purpose (since they cannot be added subunit-by-subunit in synchrony with an oligomer). Finally, mixtures of microparticles in accordance with claim 5 cannot be made using the teachings of Dower. In particular, cDNAs and genomic DNA fragments cannot be attached to microparticles through "split and mix" synthetic approaches as taught by Dower.

In view of the above differences, Applicant submits that Dower neither discloses nor suggests all the elements of the present invention. Accordingly, Applicant respectfully requests that the above rejection be withdrawn.

### Rejection under 35 U.S.C. 103

The Examiner rejected claims 7-9 under 35 U.S.C. 103(a) as being unpatentable over Dower in view of Chetverin (International patent publication WO 93/17126). The Examiner appears to argue that it would have been obvious to one of ordinary skill in the art to combine the mRNA sorting scheme of Chetverin (page 35, par. 1 & 2) for attaching polynucleotides to binary arrays with the microparticles of Dower to form mixtures of microparticles in accordance with the invention.

Applicant respectfully disagrees with the rejection, especially in view of the amendments. Dower shows the availability of a mixture of microparticles having synthetic oligonucleotides attached such that different oligonucleotides are attached to different microparticles. The purpose of the invention in Dower is the identification of combinatorially synthesized compounds. Dower neither discloses nor suggests the attachment of cDNAs or genomic DNA fragments to microparticles, or other solid phase supports. Chetverin describes the attachment of mRNA or single stranded cDNA to so-called "sectioned binary arrays." These are arrays of oligonucleotides separated from one another by barriers, such as walls, as

shown in Figures 2, 2a, 3, and 4 of the reference. Attachment of mRNA or cDNA takes place by hybridizing the mRNA or cDNA with the "binary" oligonucleotides of the array, followed by extension with a polymerase, as shown in the two embodiments of Figures 4 and 5. Chetverin calls for sectioned arrays (that is, the physical separation of the different binary oligonucleotides) so that, after hybridization and washing, amplification of mRNAs or cDNAs can take place at a particular site without mixing with mRNAs or cDNAs from adjacent sites, again as illustrated Figures 4 and 5. Neither microparticles, beads, microbeads, microspheres, nor any other type of particulate support are suggested or disclosed in Chetverin because such supports are incompatible with the objective of Chetverin's invention: namely, the creation of arrays of many discrete *and spatially addressable* populations of nucleic acid strands on a single solid phase support (e.g. see first sentence in "Summary of the Invention" section, and first paragraph of "Oligonucleotide Arrays" section). Particulate supports do not provide spatial addressability; thus, such supports would not be an obvious substitute for the sectioned arrays disclosed in Chetverin. Accordingly, Applicant's invention would not have been obvious to one of ordinary skill in the art based on Dower in view of Chetverin.

In view of the above, Applicant respectfully requests that the above rejection be withdrawn.

In view of the above, Applicants submit that the claims as written fully satisfy the requirements of Title 35 of the U.S. Code, and respectfully request that the rejections thereunder be withdrawn and the claims be allowed.

If any additional time extensions are required, such time extensions are hereby requested. If any additional fees not submitted with this response are required, please take such fees from deposit account 12-2491.

Respectfully submitted,



Stephen C. Macevicz  
Reg. No. 30,285  
Attorney for Applicants

Telephone: (510) 670-9365

Attachments:

Reissue Application Declaration by the Inventor (form PTO/SB/51)  
Supplemental Information Disclosure Statement  
Terminal Disclaimer in respect of USSN 09/092,226  
Terminal Disclaimer in respect of USSN 09/183,650  
Request to Use Computer Readable Form from Another Application  
Request to Use Formal Drawings from U.S. Patent 5,654,413  
Exhibit A